

Applicants: Michael R. Rosen, et al
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Remarks:

Reconsideration and allowance of the present application in view of the foregoing amendments and accompanying remarks are respectfully requested.

Claims 1-3, 9, 11, 15-16, and 32-35 were pending in the subject application. Claims 4-8, 10, 12, and 17-31 were withdrawn from consideration. By this Amendment, applicants have amended claims 1, 2, and 15. Accordingly, upon entry of this Amendment, claims 3, 9, 11, 16, and 32-35 and amended claims 1, 2, and 15 will be pending and under examination.

Applicants maintain that amended claims 1, 2, and 15 raise no issue of new matter and are fully supported by the specification as filed.

Support for amended claim 1 may be found inter alia in the specification, as originally filed, on page 3, line 17 through page 4, line 2; and on page 13, line 19 through page 14, line 9; and reference #56 as noted in the patent application which is incorporated by reference. Support for amended claim 2 may be found inter alia in the specification, as originally filed, on page 13, lines 15-16 and reference #56 as noted in the patent application which is incorporated by reference. Support for amended claim 15 may be found inter alia in the specification, as originally filed, on page 4, lines 3-10; and reference #56 as noted in the patent application which is incorporated by reference.

Claim Rejections-35 U.S.C. §112

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The Examiner stated that applicant's arguments in paper no. 7, filed July 7, 2003, with respect to 112 first paragraph rejection have been fully considered and are persuasive. The Examiner stated that the rejection to the claims 1-3, 9-10, and 13-16 has been withdrawn because of the amendment to claims 1, 9, and 15 and the cancellation of claims 14 and 15.

The Examiner stated, however, upon further consideration, a new ground(s) of rejection is made in view of the amendment to claims 1 and 15.

The Examiner stated that claims 1, 2, 3, 9, 11, 15, 16, 32, and 34 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. The Examiner stated that the claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected to make and/or use the invention. The Examiner stated that factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands. They include:

- (1) the quantity of experimentation necessary,
- (2) the amount of direction or guidance presented,
- (3) the presence or absence of working examples,
- (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Examiner stated that the claims are directed to assaying whether an agent affects heart rate of a cardiac cell comprising (a) contacting a cardiac cell *in vitro* with an agent to cause sustainable heart rate and (b) measuring the heart rate after step (a); (c) contacting the cardiac cell with an agent to be assayed for its effect on the heart rate and (d) measuring the heart rate after step (c) and (e) comparing the difference between step (b) and step (d).

The Examiner stated that the specification teaches measuring pacemaker current in isolated cardiac cells using transfection methods comprising contacting the isolated cardiac cells with a nucleic acid encoding HCN1, HCN2, or HCN4 or coexpressing HCN1 or HCN2 with MiRP1. The Examiner stated, however, the claims read on measuring the heart rate of a cardiac cell *in vitro* and the as-filed specification does not provide sufficient guidance or factual evidence for practicing the claimed methods. The Examiner stated that the specification does not provide a working example of the claimed method. The Examiner stated that the as-filed specification does not provide sufficient guidance and/or factual evidence to reasonably correlate using isolated cardiac cells and measuring pacemaker current to making and using an assay using a cardiac cell *in vitro* and measuring the heart rate. The Examiner stated that one skilled in the art would understand that for the claimed methods to be enabled for measuring the heart rate, a heart would have to be fully functional and the specification lacks guidance for what method steps and materials are required for one skilled in the art to use (or maintain) a heart to practice the claimed methods. The Examiner stated that the state of the art is absent for teaching how to measure heart rate in a cardiac cell *in vitro* as set forth in the claims. The Examiner stated that one skilled in the art understands that the

heart rate is the amount of heartbeats over a certain time length (e.g. minute). The Examiner stated that in view of the art of record, an *in vitro* cardiac cell cannot produce a heartbeat. The Examiner stated that the specification does not provide a sufficient guidance for reasonably correlating measuring pacemaker current to measuring heart rate of a cardiac cell *in vitro*. The Examiner stated that thus, it would take one skilled in the art an undue amount of experimentation to practice the claimed methods because the specification does not provide the method steps and materials required for measuring the heart rate of an isolated cardiac cell.

The Examiner stated that as a result, it is not apparent how one skilled in the art determines, without undue experimentation, which of the claimed methods are considered enabled, how is it apparent as to how one skilled in the art, without any undue experimentation, practices any method as contemplated by the claims, particularly given the unpredictability of making and using methods of assaying whether an agent affects heart rate using a cardiac cell that is *in vitro* and/or the doubts expressed in the art of record.

The Examiner stated that in conclusion, the as-filed specification and claims coupled with the art of record at the time the invention was made do not allegedly provide sufficient guidance and/or evidence to reasonably enable one skilled in the art to make and use any of the claimed methods. The Examiner stated that in view of the art of record that measuring a heart rate using a cardiac cell *in vitro* was considered unpredictable at the time the invention was made, and given the lack of sufficient guidance as to practice the methods cited in the

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claims, one skilled in the art would have to engage in a large quantity of experimentation in order to practice the claimed invention based on the applicant's disclosure.

In response, in an attempt to advance prosecution of the subject application, but without conceding the correctness of the Examiner's position, applicants have amended claims 1, 2, and 15.

Claim 1 has been amended to delete the term "heart rate" and have replaced the term with "beating rate." Claim 2 has been amended to delete the word "heart" and replaced it with "cardiac cell." Claim 15 has been amended to delete the term "heart rate" and have replaced the term with "beating rate." Applicants assert that an *in vitro* cardiac cell can produce a beat rate. Thus, applicants respectfully request that the Examiner reconsider and withdraw these rejections.

The Examiner stated that applicant's arguments, see paper no. 7, filed 7/7/03, with respect to 35 U.S.C. §112 second paragraph rejection have been fully considered and are persuasive. The Examiner stated that the rejection to the claims 13, 14, 15, and 16 has been withdrawn because of the amendment to claim 15 and the cancellation of claims 13 and 14. The Examiner stated that, however, upon further consideration, a new ground(s) of rejection is made in view of the addition of claims 32-35. The Examiner stated that claim 2 is rejected under 35 U.S.C. §112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner stated that claim 2 recites the limitation "the heart." The

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Examiner stated that there is insufficient antecedent basis for this limitation in the claim.

In response applicants have deleted the term "heart" in claim 2. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw this rejection because claim 2 has been amended.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

 12/19/03
Peter J. Phillips Date
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